REMARKS/ARGUMENTS

By this Amendment, claims 1, 6 and 25 are amended. Claims 1-47 are pending.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Applicants gratefully acknowledge the indication in the Office Action at page 16, paragraph 11 that claims 6-17 are free of the prior art. Accordingly, claim 6 is amended to independent form incorporating all the limitations of original claim 1 from which it originally depended, to place claims 6-17 into condition for allowance.

Rejection under 35 U.S.C. § 112

Claim(s) 1-47 stand(s) rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

(a) Recitation of "conjugated" in claims 1-47

The Office Action requires clarification of whether the term "conjugated" refers to "a covalent attachment or attachment via ionic bonds or attachment via van der Waals attractions or attachment via electrostatic attraction or etc." It would have been clear to one of ordinary skill in the art (just as it appears to be clear to the Examiner from the preceding quotation), that the term "conjugated" simply means "attached" or "bonded". While the term "conjugated" is broader than specifying the specific subclasses of attachments or bonds suggested in the preceding quotation, MPEP § 2173.04 makes it clear that "breadth of a claim is not to be equated with indefiniteness."

(b) Recitation of "free nucleobase" in claims 7 and 8

A "free nucleobase" is simply a nucleobase lacking the sugar and phosphate group present in nucleosides and/or nucleotides. This definition is in accordance with conventional meaning in the art. See Exhibit A, a definition from Dorland's Illustrated Medical Dictionary, which defines "nucleoside phosphorylase" as an enzyme that "catalyzes phosphorolysis of a nucleoside to form the free base and a ribose or deoxyribose as a step in the degradation of nucleic acids and nucleotides."

(c) Recitation of "1-200%" limitation in claims 10-17

The expressions "wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said probe nucleobases that are Watson-Crick complements to said at least one nucleobase" and "wherein said at least one nucleobase is provided in a quantity that is 1-200% of a number of said probe nucleobases that are identical to said at least one nucleobase" would be clear to one of ordinary skill in the art in view of the original disclosure, particularly in Example 1 at page 11, lines 16-19, which discloses:

> The 15-mer ssDNA Probe No. 1 contains six adenine bases. Conjugation of 2 pmoles of ssDNA Probe No. 1 with 3 pmoles of free thymine could result in 25% of the complementary A or 100% of the homologous T within Probe No. 1 bound to the added thymine.

Probe No. 1 contains 12 pmoles of A (2 pmoles of Probe x 6 A/Probe), and the blocking agent contains 3 pmoles T. Expressed in mathematical terms, 3T is 25% of 12A, wherein the percentage is based on molar concentrations.

The calculation for the homologous binding motif is analogous, and also based on molar

concentrations.

(d) Recitation of "said group" in claim 25

The amendment to claim 25, obviates this basis for the indefiniteness rejection in the manner suggested in the Office Action.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-47 as being indefinite are respectfully requested.

Rejections under 35 U.S.C. § 102

Claim(s) 1-5, 18-22, 24-26, 28-32, 34, 41, 42, 45 and 47 stand(s) rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. Patent No. 5,030,557 to Hogan et al. This rejection is respectfully traversed.

Hogan et al. discloses "helper oligonucleotides" said to bind to target nucleic acids so as to alter a secondary and/or tertiary structure of the target nucleic acid, and facilitate binding of the probe to the target (see Abstract). The helper oligonucleotide is defined at column 5, line 64 to column 6, line 4 as follows:

> [H]elper oligonucleotide: a nucleotide multimer, generally not greater than about 50 nucleotides in length, which binds the targeted nucleic acid without substantially overlapping the region bound by a nucleotide probe and which enhances the kinetics of hybridization between the probe and the sequence within the targeted nucleic acid with which it is complementary and/or which raises the Tm of the hybrid between probe and complementary sequence. [Emphasis added.]

On the other hand, base claim 1 now specifies that the at least one blocking agent comprising at least one nucleobase is conjugated to said probe hybridizing segment and/or said

target hybridizing segment prior to hybridizing said probe with said target. This is essentially the opposite of binding "the targeted nucleic acid without substantially overlapping the region bound by the nucleotide probe." Thus, Hogan's teachings of binding a helper oligonucleotide to one portion of a target nucleic acid to enhance binding of a probe to a substantially different portion of the target does not meet all the features of base claim 1 and dependent claims 4-5, 18-22, 24-26, 28-32, 34, 41, 42, 45 and 47.

The dependent claims further distinguish over Hogan et al. for at least the following additional reasons.

The helper oligonucleotide of Hogan is about 10 to about 50 nucleotides in length, whereas claim 4 specifies that the blocking agent contain up to five nucleobases and claim 5 specifies that the blocking agent contain up to two nucleobases. See Hogan et al. at column 5, lines 27-28 and 64-65.

Claim 25 specifies that the at least one blocking agent is a naturally-occurring nucleobase selected from said the group consisting of A, T, C, G and U. Hogan's disclosure of the use of DNA and RNA **containing** A, T, C, G and/or U as a helper oligonucleotide does not anticipate claim 25.

Claim 26 specifies that the at least one blocking agent is a synthetic nucleobase analogue. Hogan's disclosure of the use of synthetic DNA/RNA analogues containing base analogues as a helper oligonucleotide does not anticipate claim 26.

The passage of Hogan et al. cited in support of rejecting claim 34 does not teach

conducting detecting "under a varied condition". Hogan et al. at column 14, lines 42-46 discloses the temperature at which the assay is run. The fact that the temperature (4-5°C) varies from room temperature or the Tm of the probe:target hybrid is irrelevant to the claim limitation, which requires varying a condition while conducting the detecting step.

The passage of Hogan et al. cited by the Office Action in support of rejecting claim 42 does not teach detecting an extent of complementarity between the probe and the target.

Accordingly, reconsideration and withdrawal of the rejection of claim(s) 1-5, 18-22, 24-26, 28-32, 34, 41, 42, 45 and 47 as being anticipated by Hogan et al. are respectfully requested.

Claim(s) 1, 23, 27, 43-44 and 46 stand(s) rejected under 35 U.S.C. § 102(e), as allegedly being anticipated by U.S. Patent No. 6,312,925 to Meyer, Jr. et al. This rejection is respectfully traversed.

Meyer discloses "methods and compositions for efficient targeting and modification of target sequences in duplex DNA . . . utilizing oligonucleotides or oligonucleotide compositions containing two domains." See Abstract. The Office Action interprets the target of Meyer to be the target of claim 1, the oligonucleotide of Meyer to be the probe of claim 1 and the modifying agent of Meyer to be the blocking agent of claim 1. However, Meyer does not disclose or suggest that these modifying agents or modifying groups contain at least one nucleobase, as required by base claim 1. See, e.g., Meyer at column 14, line 8 to column 15, line 25, which discloses that the modifying groups are "reactive groups that are able to form covalent bonds between the oligonucleotide and the target sequence" or are groups capable of reacting "with a

specific functional group of a nucleotide in the target sequence, to generate a pre-mutagenic lesion in the target sequence."

Accordingly, reconsideration and withdrawal of the rejection of claim(s) 1, 23, 27, 43-44 and 46 as being anticipated by Meyer, Jr. et al. are respectfully requested.

Claim(s) 1, 4, 5, 29-31 and 39 stand(s) rejected under 35 U.S.C. § 102(e), as allegedly being anticipated by U.S. Patent No. 6,130,038 to Becker et al. This rejection is respectfully traversed.

Becker et al. discloses "oligonucleotides containing one or more modified nucleotides which increase the binding affinity of the oligonucleotides to target nucleic acids having a complementary nucleotide base sequence." See Abstract. Becker et al. at columns 9-10 discloses "conjugate molecules attached to oligonucleotides ... may function to further increase the binding affinity and hybridization rate of these oligonucleotides to target." These conjugate molecules can themselves be oligonucleotides. Becker et al. at column 9, lines 63-65. These conjugate oligonucleotides are later referred to as "helper probes" and "helper oligonucleotides" at column 10, lines 17 and 45, column 11, lines 19, and column 13, lines 46-47. These are the same "helper oligonucleotides" disclosed by Hogan et al. See Becker et al. at column 11, lines 19 and column 13, lines 46-47. Becker et al. differs from Hogan et al. in this regard in that Becker et al. teaches the use of certain modified nucleotides within the oligonucleotides with or without the helper oligonucleotides. Thus, Becker et al. fails to anticipate the claimed invention for at least the same reasons as Hogan et al. shown above.

Furthermore, the Office Action has further misinterpreted the teachings of Becker et al.

with respect to claims 4 and 5. References in Becker et al. to modification of 4 or 5 consecutive nucleotides do not mean that the "helper oligonucleotide" is 4 or 5 nucleotides in length. Rather, the cited passages at column 8, lines 53-63 and column 21, lines 42-48 refer to nucleotides of the probe having, e.g., modified ribofuranosyl rings. Becker et al. does not describe how long the "helper oligonucleotides" can be, although it provides examples of 31 to 41 nucleotides in length (column 34, lines 49-51) and incorporates by reference the teachings of Hogan et al., which defines "helper oligonucleotides" as being about 10 to about 50 nucleotides in length. See Becker et al. at column 11, lines 19-23 and Hogan et al. at column 5, lines 27-28 and 64-65.

Accordingly, reconsideration and withdrawal of the rejection of claim(s) 1, 4, 5, 29-31 and 39 as being anticipated by Becker et al. are respectfully requested.

Rejections under 35 U.S.C. § 103

Claim(s) 32-34, 36-38 and 40 stand(s) rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hogan et al. in view of U.S. Patent No. 6,048,690 to Heller et al. This rejection is respectfully traversed.

Hogan et al. fails to meet all the features of claims 32-34, 36-38 and 40 for at least the same reasons, noted above, that it fails to anticipate base claim 1. Although the Office Action appreciates that Hogan et al. fails to disclose "analyzing an electronic characteristic of said complex" as specified in claim 33, the Office Action fails to appreciate Hogan's failure to disclose that at least one blocking agent comprising at least one nucleobase is conjugated to said probe hybridizing segment and/or said target hybridizing segment prior to hybridizing said probe with said target. Regardless of whether Heller et al. teaches anything regarding analyzing

electronic characteristics of samples, the Office Action fails to show how one of ordinary skill in the art would have been motivated with a reasonable expectation of success to modify the teachings of Hogan et al. with the teachings of Heller et al. to reach the claimed invention, wherein at least one blocking agent comprising at least one nucleobase is conjugated to said probe hybridizing segment and/or said target hybridizing segment prior to hybridizing said probe with said target.

Moreover, measuring an increase in fluorescent intensity (the "Fluorescent Perturbation Effect or FPE), as the first fluorescent manifestation caused by the electronic denaturation and electrophoresis of DNA hybrids (Heller et al. at column 4, lines 57-62) is not "analyzing an electronic characteristic of said complex" as specified in claim 33. Fluorescent intensity is not an electronic characteristic of a complex, as used in claim 33.

Accordingly, reconsideration and withdrawal of the rejection of claim(s) 32-34, 36-38 and 40 as being obvious over Hogan et al. in view of Heller et al. are respectfully requested.

Claim(s) 35 stand(s) rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hogan et al. in view of U.S. Patent No. 5,846,729 to Wu et al. This rejection is respectfully traversed.

Hogan et al. fails to meet all the features of claim 35 for at least the same reasons, noted above, that it fails to anticipate base claim 1. Although the Office Action appreciates that Hogan et al. fails to disclose detecting a complex under varied photonic conditions as required by claim 35, the Office Action fails to appreciate Hogan's failure to disclose that at least one blocking agent comprising at least one nucleobase is conjugated to said probe hybridizing

segment and/or said target hybridizing segment prior to hybridizing said probe with said target. Regardless of whether Wu et al. teaches anything regarding altering photonic conditions of a test medium, the Office Action fails to show how one of ordinary skill in the art would have been motivated with a reasonable expectation of success to modify the teachings of Hogan et al. with the teachings of Wu et al. to reach the claimed invention, wherein at least one blocking agent comprising at least one nucleobase is conjugated to said probe hybridizing segment and/or said target hybridizing segment prior to hybridizing said probe with said target.

Accordingly, reconsideration and withdrawal of the rejection of claim(s) 35 as being obvious over Hogan et al. in view of Wu et al. are respectfully requested.

Acknowledgment of IDS

Applicant has not received an initialed copy of the Form PTO-1449 filed January 3, 2003. Since the PTO's PAIR system does not evidence any receipt of this document, Applicants enclose copies of the corresponding IDS as Exhibit B, including the Form PTO-1449 and references cited, as well as a copy of the date-stamped receipt therefor. Applicants respectfully request record consideration of the references cited in the IDS.

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

By _____

June 17, 2003

Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.

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EXHIBIT A

nu·cleo·side phos·phor·y·lase

Any of the enzymes of the sub-subclass pentosyltransferases [EC 2.4.2] that catalyz phosphorolysis of a nucleoside to form the free base and a ribose (or deoxyribose) as a step in the degradation of nucleic acids and nucleotides. See also purine-nucle phosphorylase and pyrimidine-nucleoside phosphorylase.

EXHIBIT B